REMARKS

Applicant acknowledges with appreciation the statement in the Office Action that claims 4, 14 and 18 are allowable, and that claims 6-10 would be allowable if amended to incorporate the changes suggested in the Office Action.

Claims 6-10 stand rejected under 35 U.S.C. § 112, 2nd paragraph, on the grounds that they are indefinite for omitting essential steps. In response, Applicant has herein amended these claims to insert the meaning of the steps represented as a-f in the original claims. As acknowledged in the Office Action, the steps for obtaining the intermediates and final products are disclosed in the specification, and therefore these amendments to the claims do not represent new matter. In view of this, Applicant respectfully requests withdrawal of the rejection of claims 6-10 under 35 U.SC. § 112, 2nd paragraph.

The Office Action states that claims 2, 7 and 12 stand rejected under 35 U.S.C. § 102(b) as anticipated by Spath et al., pointing to the entire disclosure and particularly compound I on pages 189 and 191. Claim 2 is directed to a particular resveratrol derivative (compound 14g in the specification); claim 7 is directed to a method for synthesizing the compound of claim 2; and claim 12 is directed to a pharmaceutical composition incorporating the compound of claim 2 or a salt thereof. This rejection has been carefully considered and is respectfully traversed for the reasons discussed below.

The English abstract of the Spath publication, which is in the German language, discloses the compound phenol, 4-[2-3,5-dimethoxyphenyl)ethenyl; the compound shown in the abstract

and on page 189 is not identical to the compound claimed in claim 2. The compound of claim 2 is in cis formation, whereas the stereochemistry is not shown for the compound shown in Spath, and one of ordinary skill in the art would understand that Spath's compounds would be in the trans formation, given that Spath's compounds are obtained from and/or derived from a plant material, namely red sandalwood. Although an English translation of the entire reference has not been obtained, the title set forth in the English abstract is "Constituents of red sandalwood....", and thus it appears that the reference discloses derivatives of these "constituents", and these derivatives are also shown without any indication of their stereochemistry.

Applicant notes that one of ordinary skill in the art understands that stilbenes obtained isolated from plant materials are in the trans form, because plants tend to make trans form of these compounds, which are considerably more stable than cis-stilbenes. Further, one of skill in the art appreciates that the trans form is the preferred geometric configuration of stilbenes. In the early 1940's, at the time of Spath's publication, any disclosure of stilbene compounds isolated from the natural source of plants would necessarily be considered to be in the trans formation. From this it is apparent that any derivatives of the naturally occurring stilbene disclosed in Spath would also be in trans form. As reflected in Applicant's specification, it is not an easy task to transform the trans compound into a cis compound, and there is no indication in the English abstract of this reference that such a transformation was performed, nor is there any suggestion to do so.

The present invention stems in part from the inventors' discovery that by creating cis forms of the derivatives of certain natural compounds, once could create cis stilbene compounds having properties far superior in certain activity than the natural trans stilbenes or their trans stilbene derivatives. The present invention relates in part to a novel and unobvious particular modified Wittig reaction, which permits the creation of the object cis compounds; if this reaction is not utilized, attempts to make derivatives of trans compounds would result in trans compounds. Additionally, neither the synthesis method recited in claim 7 nor the composition recited in claim 12 is disclosed or even suggested in the cited Spath reference.

In view of the foregoing, Applicant most respectfully requests withdrawal of the rejection of claims 2, 7 and 12 under 35 U.S.C. § 102(b) over Spath et al.

Claims 1 and 2 stand rejected under 35 U.S.C. § 102(b) over Takaoka. The Office Action points to pages 405-407, particularly to compound VIII on page 406. This rejection has been carefully considered, and is respectfully traversed. As discussed above with respect to the Spath et al. reference, Takaoka fails to disclose or suggest compounds in the cis formation. Although Takaoka's compound VIII appears to have the same structure as Applicant's compound claimed in claim 2, again, no stereochemistry is disclosed or suggested by Takaoka. Takaoka clearly discusses that Takaoka's compounds are obtained from natural plant sources, and/or are synthesized derivatives of these compounds from natural plant sources. As in Spath et al., there is no discussion in Takaoka regarding cis compounds, and one of skill in the art would understand that Takaoka at best discloses trans compounds but does not disclose the claimed cis

compounds. Finally, although claim 1 is rejected under § 102(b) Takaoko, it does not appear that a compound having the chemical formula required by the compound of claim 1 is disclosed by this reference, and certainly the particular cis isomer claimed is not disclosed.

In view of the foregoing, reconsideration and withdrawal of the rejection of claims 1 and 2 under 35 U.S.C. § 102(b) over Takaoka is most respectfully requested.

Claims 1, 11 and 15 stand rejected under 35 U.S.C. § 102(a) over Ghai et al. (US application publication no. 2002/0028852 A1). The Office Action alleges that this reference teaches the claimed cis compound and composition, and points to paragraphs 0003, 0012, 0016, 0017, 0019 and Table 1. Applicant respectfully traverses this rejection for the reasons discussed below.

The Ghai application fails to disclose the claimed compound, or the composition including the compound of claim 1, or the method of treatment using the compound of claim 1, as is urged in the Office Action. Although Ghai discloses several derivatives of resveratrol (see, for example, paragraphs 0013 and 0016), the specific compound set forth in claim 1, which is 3-hydroxy-4',5'-dimethoxy stilbene is not disclosed by Ghai, let alone the cis form of this compound as is required by Applicant's claim 1. Moreover, Ghai fails to suggest modification of its own compounds to achieve the presently claimed compound.

Accordingly, Applicant most respectfully requests reconsideration and withdrawal of the rejection of claims 1, 11 and 15 under 35 U.S.C. § 102(a) over Ghai et al.

Claims 3 and 13 stand rejected under 35 U.S.C § 103(a) as unpatentable over Gracza. The Office Action states that one of skill in the art would have found the claimed compound and composition obvious over Gracza' compound trans form of the compound (described by the English abstract of Gracza as 1,3-benzodiol, 5-[2-(4-methoxyphenyl)ethenyl]), on the grounds that compounds which have very close structural similarities are expected to have similar properties absent a showing of unexpected results.

In response, Applicant notes that its specification illustrates that its cis compound, set forth in claim 3, exhibits different levels of cytotoxicity, as compared to the trans form of the compound. In this regard, see Table 1 on page 28 of Applicant's specification, which shows that the trans form (compound 14l) exhibits different levels of cytotoxicity with respect to various cancer cell lines, as compared with the claimed cis form (compound 14k). For example:

-with respect to the Leukemia P388 cell line, the trans form (14l) is 28.9 $ED_{50}\mu g/mL$, whereas the cis form (14k) is 2.75 $ED_{50}\mu g/mL$; thus, the trans form is about 14x less active than the cis form in terms of cytoxicity for this cell line; and

-with respect to the CNS SF-268 cell line, the trans form (14l) is 3.1 $ED_{50}\mu g/mL$, whereas the cis form (14k) is 15.6 $ED_{50}\mu g/mL$; thus the trans form is about 5x more active than the cis form in terms of cytotoxicity for this cell line.

Thus, Applicant's specification illustrates that compounds which are similar structurally do not necessarily have similar properties, and therefore one of ordinary skill in the art would not expect from Gracza's teaching of its own trans compound that a cis compound would have the

same activity as Applicant's cis compounds. Moreover, there is nothing in the English abstract of Gracza (note that Applicant has not obtained and reviewed an English translation of the Gracza reference) which would have suggested or otherwise motivated one of skill to modify Gracza to create the presently claimed cis compound. Again, it was Applicant's invention to create very specific cis derivatives of resveratrol, in order to create compounds which would show promise as effective anti-neoplastic compounds. To create these cis derivatives, Applicant also had to construct its specifically described synthesis method previously not used to create such derivatives.

In view of the foregoing, reconsideration and withdrawal of the rejection of claims 3 and 13 under 35 U.S.C § 103(a) as unpatentable over Gracza is most respectfully requested.

Claims 3, 13 and 17 stand rejected under U.S.C § 103(a) as unpatentable over Ryu et al. The Office Action urges that Ryu teaches the trans isomer of the instant compound, referring to the entire disclosure and page 43, which is said to have anti-tumor activity, and therefore the claimed compound, composition and method of treatment would have been obvious due to the close structural similarity of Ryu's compounds. This rejection has been carefully considered, and is also traversed, for similar reasons to that set forth in response to the rejection of certain claims over the Gracza reference.

Ryu discloses on page 43, as its Compound I, 3,5-dihydroxy-4'-methoxystilbene. This compound must be in the trans form, as it is obtained from "commercially available plant materials" (see page 42, right hand column, first sentence under the heading "Extraction and

Isolation"), which as discussed above in this Response are composed of trans compounds. In fact, Ryu confirms the trans structure of Ryu's compounds on page 43, under its "Results and Discussion", lines 19 et seq., where it states "it seemed that the trans-stilbene skeleton of them rather than the substituent groups was more responsible to the antitumor activity" (emphasis added). As discussed above with respect to the § 103(a) rejection over Gracza ,Applicant's specification illustrates that compounds which are similar structurally do not necessarily have similar properties. Therefore one of ordinary skill in the art would not expect from Ryu's teaching of its trans compounds that a cis compound would have the same activity as Applicant's cis compounds. Significantly, there is nothing in Ryu which would have suggested or otherwise motivated one of skill in the art to modify Ryu's trans compounds, let alone any suggestion or teaching of a synthesis method, to create the presently claimed cis compound, let alone the presently claimed composition and method of use.

Claims 1, 11 and 15 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Gaih et al. In support of this rejection, the Office Action states that one of skill in the art would have found the claimed compound, composition and method of use obvious, because the compound Ghai teaches has anticancer activity. This rejection is traversed respectfully.

Applicant acknowledges that Ghai discloses several derivatives of resveratrol (see, for example, paragraphs 0013 and 0016) and Ghai states that some or all of its compounds are useful for preventing or treating cancer. Nonetheless, this rejection must be withdrawn, because there is nothing in Ghai which would have led one of skill in the art to create Applicant's very specific

compound set forth in claim 1, nor does Ghai in any way teach the synthesis method required to create same or even to create cis analogs of Ghai's own compounds. Ghai simply fails to teach or suggest to one of skill in the art Applicant's modified Wittig reaction that is required to create its claimed compound, composition and method of use. Accordingly, reconsideration and withdrawal of this rejection is most respectfully requested.

Claims 1, 2, 11 and 12 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Takaoka. This rejection has been carefully considered, and is most respectfully traversed. Takaoka fails to disclose or suggest the desirability of compounds in the cis formation. Further, Takaoka fails to disclose, teach or suggest how to modify its own compounds to produce cis compounds. Takaoka fails to illustrate any recognition of differences between stereoisomers of its compound. As noted previously, Takaoka clearly discusses that the compounds described therein are obtained from natural plant sources, and/or are synthesized derivatives of these compounds from natural plant sources. Thus, one of skill in the art would understand that Takaoka at best discloses trans compounds, not the claimed cis compounds.

Further, Takaoka does not discuss use of its own compounds, or of any compounds for that matter, for use in treating humans or animals or in a pharmaceutical compositions.

In view of the foregoing, reconsideration and withdrawal of the rejection of claims 1, 2, 11 and 12 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Takaoka is respectfully requested.

Claims 1-3, 11-13 and 15-17 stand rejected under 35 U.S.C. § 102(a) as unpatentable over Soby et al. In support of this rejection, the Office Action states that Soby teaches resveratrol analogs which may contain methoxy and hydroxyl substituents, and may include both cis and trans isomers. The Office Action points in particular to paragraphs 0014-0015, 0019 and claims 1, 6, 8, 11 and 14-16 of Soby. This rejection has been carefully considered and is respectfully traversed, for the reasons discussed below.

The Soby reference fails to provide enablement for even a single one of any of the wide number of compounds it purports to disclose and claim. There is nothing in Soby which teaches anything about making any of Soby's compounds which would fall within its generic formula, let alone teach how to make any of Applicant's claimed compounds. Furthermore, there is nothing in the reference which would teach or suggest to anyone how to make or use the presently claimed compounds, which are made by a particularly defined process.

Soby states at the end of paragraph 0015 that its compounds can be in cis or trans configuration, without providing any teaching as to whether one or the other would have better results, effectively equating cis and trans isomers of its compounds, which is in direct contrast to the evidence at hand. Thus, no differentiation is made in Soby between the cis and trans versions of its compounds. As discussed above in this Response, there is not necessarily predictability with respect to the activity of what stilbene compounds having potentially similar structures. Certainly there is no motivation within Soby as to how to choose one of its covered compounds versus another, let alone how to create any of the compounds.

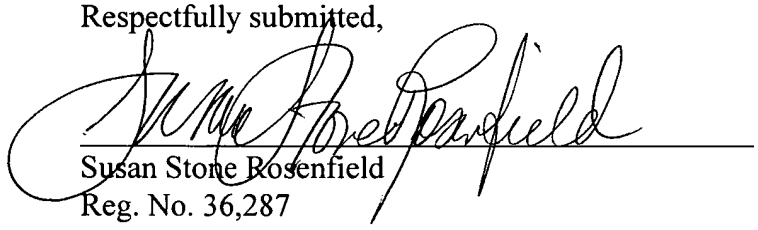
It should also be noted that one of skill in the art of methods of treatment for cancer would not find motivation within Soby in any event, given that Soby's specification (although mentioning in paragraph 0007 that resveratrol analogs in general may be used as carcinogenesis inhibiting agents) and claims are clearly directed to anti-aging treatments for skin (see paragraphs 0016 and 0017 which teach its benefits, none of which are for cancer treatment

Accordingly, Applicant requests reconsideration and withdrawal of the rejection of Claims 1-3, 11-13 and 15-17 stand rejected under 35 U.S.C. § 102(a) as unpatentable over Soby.

SUMMARY

In view of the foregoing, Applicant most respectfully requests allowance of the claims. The Examiner is invited to telephone Applicant's undersigned representative, if she believes that it would facilitate prosecution.

Respectfully submitted,



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I hereby certify that this paper and any documents referred to as herein are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on **November 16, 2006**.

Rebecca L. Camelio

Rebecca L. Camelio, IP Legal Assistant

November 16, 2006
Date of Signature